Treatment of Recurrent or Progressive Malignant Glioma with a Recombinant Adenovirus Expressing Human Interferon-Beta (H5.010CMV*hIFN*-β): A Phase I Trial (UPCC#: 2399)

NON-TECHNICAL ABSTRACT

Primary brain tumors in adults, principally the anaplastic astrocytoma and glioblastoma multiforme, are highly malignant and nearly always fatal. Advances in surgical techniques and in radiation therapy have had minimal impact on either survival or the improvement in quality of life in patients with such tumors. The primary objective of this study is to determine the toxicity of intratumoral injection of a recombinant adenovirus expressing human interferon-beta in patients with recurrent or progressive anaplastic astrocytoma or glioblastoma multiforme.

Direct injection of the adenoviral vector expressing human interferon-Beta may limit systemic exposure to the therapeutic agent and, therefore, minimize systemic toxicity. Local delivery of the vector to the tumor will achieve high concentrations of the therapeutic agent within the tumor. This will be achieved by stereotactic injection of the vector into the brain tumor at Day 1 and by infiltration of the tumor with the vector at the time of subsequent gross total resection of the tumor (at Day 8). The local production of the interferon protein following gene transfer has tumoricidal effects in animal models and extends beyond those cells that have received the vector. This could be important to reach sections of the remaining tumor that cannot easily be resected by the neurosurgery performed at Day 8.

The toxicity and antitumor efficacy of H5.010CMV*hIFN-β* has not been previously studied in humans, although preliminary toxicology studies in rodents and non-human primates suggests that this approach can be safely undertaken. Our prior adenovirus based delivery of the herpes virus thymidine kinase gene (H5.010RSV-tk) using a similar adenoviral vector was generally well tolerated in patents with malignant gliomas using a similar clinical trial design. This present study will demonstrate the safety of this therapeutic approach, provide information on the most common adverse events and has the potential to demonstrate efficacy in patients with an otherwise incurable advanced malignancy.